

03-08-00

A

03/07/00
jc682 U.S. PTO**UNITED STATES PATENT APPLICATION TRANSMITTAL FORM**BOX PATENT APPLICATION
ASSISTANT COMMISSIONER FOR PATENTS
WASHINGTON, D.C. 20231

Docket No.: 680.0035USU

jc675 U.S. PTO
09/521442
03/07/00

Sir:

Transmitted herewith for filing is the patent application of

Inventor: Gopinathan K. Menon

For: METHOD OF TREATING SKIN CONDITIONS

Enclosed are:

XXX Specification (24 pps) including: Description (18 pps); Claims (5 pps); Abstract (1pp);**XXX** 2 sheets of drawings;**XXX** Declaration and Power of Attorney;**XXX** An assignment of the invention to: **Avon Products, Inc.** including \$40.00 recordation fee and Assignment Recordation Form Cover Sheet;

Information Disclosure Statement (with copies of patent);

Form - PTO-1449;

Verified Statement Claiming Small Entity Status; and

Priority of Provisional Patent Application Serial No. _____, filed on _____, in _____ is claimed under 35 U.S.C. §119.

The Filing Fee is calculated below.

CLAIMS AS FILED				
(1) For	(2) Number Filed	(3) Number Extra	(4) Rate	(5) Basic Fee \$690.00
Total Claims	20 - 20 =	0	0 x \$18.00	\$0.00
Independent Claims	4 - 3 =	1	1 x \$78.00	\$78.00
Multiple Dependent Claim Fee			x \$270.00 = \$0.00	
TOTAL FILING FEE			\$768.00	

1/2 FILING FEE FOR SMALL ENTITY	\$
---------------------------------	----

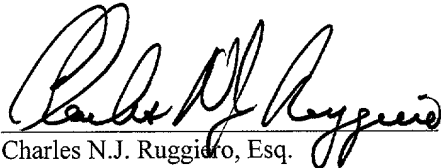
XXX A check in the amount of \$ **808.00** to cover the filing fee (\$768.00) and recordation fee (\$40.00) is enclosed.

XXX The Commissioner is hereby authorized to charge any additional fees under 37 C.F.R. §§1.16 and 1.17 which may be required with this communication or during the entire pendency of the application, or credit any overpayment, to **Deposit Account No. 01-0467**. A duplicate copy of this Form is enclosed.

Address all future communications to:

Charles N.J. Ruggiero, Esq.
Ohlandt, Greeley, Ruggiero & Perle
One Landmark Square, 9th Floor
Stamford, Connecticut 06901-2682
U.S.A.

March 7, 2000
Date of Signature

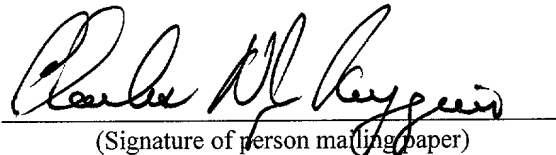


Charles N.J. Ruggiero, Esq.
Registration No. 28,468
Attorney for Applicant
Ohlandt, Greeley, Ruggiero & Perle, L.L.P.
One Landmark Square, 9th Floor
Stamford, CT. 06901-2682
Tel (203) 327-4500
Fax (203) 327-6401

CERTIFICATE OF EXPRESS MAILING

I hereby certify that this paper or fee is being deposited with the United States Postal Service "Express Mail Post Office to Addressee" Certificate No. **EL470232118US**, service under 37 CFR §1.10 and is addressed to: Box Patent Application, Assistant Commissioner for Patents, Washington, D.C. 20231 on March 7, 2000.

Charles N.J. Ruggiero
(Typed name of person mailing paper)


(Signature of person mailing paper)

004060 344T2360

METHOD OF TREATING SKIN CONDITIONS**BACKGROUND OF THE INVENTION**1. Field of the Invention

5 The present invention relates to topical compositions and methods useful to prevent, ameliorate or treat skin and other conditions associated with upregulation of genes in skin cells that respond to activation of Peroxisome Proliferator Activated Receptors (hereinafter "PPAR"), which are proteinaceous. More particularly, the present invention relates to topical compositions and methods useful to prevent, ameliorate or treat conditions, such as acne and/or cellulite, associated with upregulation of PPAR.

2. Description of the Related Art

10 Although the role of PPAR in metabolic pathways is still under investigation, it is known that PPAR receptors have a fundamental role in regulating energy balance, particularly via glucose and lipid metabolism. In addition, it is known that
20 there is not a single PPAR but, instead, a family, or isoforms, of PPAR: PPARalpha, PPARGamma and PPARbeta/sigma.

U.S. Patent No. 6,004,741 to Rosenfield discusses PPAR in sebocyte development, and suggests that PPAR, particularly PPARgamma, may be useful with respect to conditions associated with increased sebum production, such as *acne vulgaris*. In addition, U.S. Patent Nos. 5,994,554 to Kliewer et al.; 5,939,442 to Evans et al.; and 5,981,586 to Pershadsingh, disclose methods to either identify compounds that interact with or modify PPARgamma mediated pathways.

It has been reported that feeding perilla oil to rats reduces visceral adipose tissue by down-regulating adipose cell/tissue differentiation. Okuno et al. J. Nutr. 127: 1752 - 1757 (1997). Another study in which Japanese Quails were fed perilla oil demonstrated a reduction in plasma lipid levels and foam cells in the aorta. Reducing both plasma lipid levels and aortic foam cells reduces atherosclerosis.

As can be understood by those in the art, compositions that require systemic administration are particularly undesired when treating skin conditions. This is simply because systemic administration provides greater opportunity for an active to interact at receptor sites away from the target site. Non-target receptor activity results in undesired side effects.

U.S. Patent No. 5,312,834 to Yeo teaches compositions for the treatment of acne. The Yeo patent exemplifies topical compositions having both eicosapentaenoic acid and alpha-linolenic acid, preferably in a weight ratio of 1:0.1 to 20, respectively. Although Yeo teaches that perilla oil contains alpha-linolenic acid and fish oil contains eicosapentaenoic acid, Yeo fails to teach or suggest that perilla oil would be effective to treat acne, absent the required ratio of eicosapentaenoic acid to alpha-linolenic acid.

U.S. Patent No. 5,997,852 to Yoneda et al. provides an oral remedy for dermatitis that comprises both a zinc compound and a compound that may be either a multivalent unsaturated fatty acid or an ester thereof. Example 8 of the Yoneda et al. patent teaches a formulation comprising zinc sulfate and perilla oil as a source of linoleic acid. However, the Yoneda et al. patent fails to suggest that perilla oil is an effective topically active ingredient to prevent, ameliorate or treat acne or a non-diseased state, i.e. cosmetic, skin condition.

Thus, the prior art fails to disclose or suggest the use of topical compositions having perilla oil in an amount effective to improve the cosmetic appearance of skin by preventing, ameliorating or treating acne and/or non-disease state skin

conditions, such as cellulite, that are associated with upregulation of PPAR mediated pathways.

SUMMARY OF THE INVENTION

5 It is an object of the present invention to provide a method of preventing, treating or ameliorating an affected area of the skin or hair.

10 It is another object of the present invention to provide a method of improving the aesthetic appearance of an affected, but non-disease state, area of the skin or hair that exhibits characteristics associated with conditions, such as blemishes, skin breakouts, cellulite, oily skin, oily hair, oily scalp, and combinations thereof.

15 It is yet another object of the present invention to provide a method of treating a skin or hair condition resulting from or accompanied by an upregulation of PPAR receptors.

20 The present invention, in brief summary, is topical compositions having at least one PPAR Stabilizer, and methods of administering such topical compositions to improve the condition and aesthetic appearance of such affected skin and/or hair.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 illustrates the results of Example 1; and

Figure 2 illustrates the results of Example 2.

5 DETAILED DESCRIPTION OF THE INVENTION

10 A "topical composition" as used herein refers to a composition intended to be directly applied or spread on the surface of skin and/or hair and scalp. An "effective amount" means an amount of a compound or a composition sufficient to induce a positive change in the skin and/or hair condition. A "physiologically acceptable vehicle" or a "suitable topical vehicle" refers to a cosmetic, medicament or inert ingredient that is suitable for use in direct contact with human tissues without undue toxicity. All percentages refer to weight percent based on the total weight of the topical composition.

15 The first principal component of the present invention is an inhibitor of PPAR upregulation (hereinafter "PPAR Stabilizer"). The term PPAR Stabilizer as used herein
20 encompasses all compounds that inhibit upregulation of genes that respond to activation of PPAR proteins via agonists, but do not effect basal levels of PPAR activity. In other words, the PPAR Stabilizer competes with the agonist that upregulates PPAR

activity. The differentiation between upregulated and normal PPAR activity will be discussed below.

The preferred PPAR Stabilizer is perilla oil, especially perilla seed oil. Perilla seed oil contains a highly unsaturated drying oil similar to linseed oil. It is surprising and unexpected that perilla oil inhibits upregulation by PPAR agonists, as perilla oil itself contains PPAR agonists such as linolenic acid and linoleic acid. This may be attributable to perilla oil undergoing oxidation on storage due to the high content of unsaturated fatty acids. The oxidation process may alter the PPAR stimulating activity of linolenic acid and linoleic acid, causing the acids to bind to and shield the receptors, but not activate them, thereby preventing other agonists from reaching and activating the receptors.

In addition to the PPAR Stabilizer, the present invention may include a secondary component. The secondary component is selected from one or more of the following eleven groups.

1. Retinoids and Reginoids: Examples of suitable retinoids include retinol, retinoic acid, retinyl palmitate, retinyl propionate, retinyl acetate, isotretinoin as well as synthetic retinoid mimics, and derivatives of the foregoing, as

well as others that bind to RAR receptors. Retinoids include compounds, such as all-trans retinoic acid, 9-cis retinoic acid, phytanic acid and others that bind to RXR receptors.

5 2. An estrogen synthetase (aromatase) stimulating compound: Examples of such a compound include caffeine and/or derivatives thereof, and any mixture thereof. Caffeine is the more preferred of such compounds.

10 3. A compound capable of inhibiting 5 alpha-reductase activity: Examples of such a compound include linolenic acid, linoleic acid, finasteride, and mixtures thereof.

15 4. An exfoliation promoting compound: Suitable examples include alpha hydroxy acids; beta hydroxy acids; oxa acids as disclosed in U.S. Patent No. 5,847,003 (the disclosure of which is incorporated herein by reference); oxa diacids as disclosed in U.S. Patent No. 5,834,513 (the disclosure of which is incorporated herein by reference); mechanical exfoliation
20 compounds, such as bamboo exfoliant extract; salicylic acid; benzoyl peroxide; keto acids, such as pyruvic acid, 2-oxopropanoic acid, 2-oxobutanoic acid, and 2-oxopentanoic acid; and mixtures thereof.

The preferred exfoliation promoting compounds are lactic acid, glycolic acid, 3,6,9-trioxaundecanedioic acid, and any mixture thereof. When the present invention includes an exfoliation promoting compound, the composition comprises about 1 wt% to 20 wt%, preferably about 1 wt% to about 15 wt%, more preferably about 4 wt% to about 10 wt% acid, and most preferably about 4 wt% of the exfoliation promoting compound.

5. An ultraviolet (UV) light protecting/sunscreen agent:

Examples include organic and inorganic sunscreens, such as titanium dioxide, zinc oxide, methyl benzylidene camphor and/or its derivatives, octocrylene, anthranilates, benzophenones, butylmethoxydibenzoylmethane (avobenzene), naphtholsulphonates, benzoic acid derivatives, salicylates, cinnamic acid derivatives, terephthalylidene dicamphor sulfonic acids, and mixtures thereof. Of these, butylmethoxydibenzoylmethane, octocrylene, octylsalicylate, octylmethoxycinnamate and oxybenzone, and mixtures thereof are preferred. Butylmethoxydibenzoylmethane, oxybenzone, octylmethoxycinnamate, terephthalylidene dicamphor sulfonic acids, and mixtures thereof are most preferred. Salts, esters and other derivatives of the aforementioned sunscreen agents, which are compatible with the composition, are also contemplated in practicing the present invention. Co-formulation with an ultraviolet light

protecting/sunscreen agent is particularly desirable when the present invention is prepared for consumers who engage in outdoor activities.

5 6. Barrier function enhancing agents: Examples include
ceramides; essential fatty acids and their esters, especially
glycerides, α -hydroxy fatty acids and their esters, ω -hydroxy
fatty acids and their esters; phospholipids; cholesterol and its
esters, such as cholesteryl hemisuccinate, cholesteryl
10 phosphate; and cholestanol and its derivatives. The barrier
function enhancing agent can be added to a topical composition
either as singular molecular entities or as a complex mixture of
lipids derived from either synthetic, animal or plant sources.

15 7. Collagen enhancing agents: These agents prevent skin
sagging by promoting a net increase in collagen, either by
reducing collagen breakdown or by promoting collagen formation.
Examples of such agents include *Clara* extract (*Sophora*
augustifolia), ascorbyl-phosphoryl-cholesterol, ascorbic acid,
20 ascorbic acid derivatives, and mixtures thereof.

8. Elastase inhibitors: Examples of these inhibitors include fatty acids, such as oleic acid, perinanic acid, and Honeysuckle extract (*Lonicera caprifolium*). These inhibitors act to prevent sagging of the skin.

5

9. Skin lightening agents: Examples include kojic acid, hydroquinone, licorice derivatives, ascorbic acid/ascorbic acid derivatives (e.g. magnesium ascorbyl phosphate), arbutin, bearberry (*Arctostaphylos uva ursi*), *Glycyrrhiza glabra* and its derivatives, *Chlorella vulgaris* extract, and mixtures thereof.

10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60
61
62
63
64
65
66
67
68
69
70
71
72
73
74
75
76
77
78
79
80
81
82
83
84
85
86
87
88
89
90
91
92
93
94
95
96
97
98
99
100
101
102
103
104
105
106
107
108
109
110
111
112
113
114
115
116
117
118
119
120
121
122
123
124
125
126
127
128
129
130
131
132
133
134
135
136
137
138
139
140
141
142
143
144
145
146
147
148
149
150
151
152
153
154
155
156
157
158
159
160
161
162
163
164
165
166
167
168
169
170
171
172
173
174
175
176
177
178
179
180
181
182
183
184
185
186
187
188
189
190
191
192
193
194
195
196
197
198
199
200
201
202
203
204
205
206
207
208
209
210
211
212
213
214
215
216
217
218
219
220
221
222
223
224
225
226
227
228
229
230
231
232
233
234
235
236
237
238
239
240
241
242
243
244
245
246
247
248
249
250
251
252
253
254
255
256
257
258
259
260
261
262
263
264
265
266
267
268
269
270
271
272
273
274
275
276
277
278
279
280
281
282
283
284
285
286
287
288
289
290
291
292
293
294
295
296
297
298
299
300
301
302
303
304
305
306
307
308
309
310
311
312
313
314
315
316
317
318
319
320
321
322
323
324
325
326
327
328
329
330
331
332
333
334
335
336
337
338
339
340
341
342
343
344
345
346
347
348
349
350
351
352
353
354
355
356
357
358
359
360
361
362
363
364
365
366
367
368
369
370
371
372
373
374
375
376
377
378
379
380
381
382
383
384
385
386
387
388
389
390
391
392
393
394
395
396
397
398
399
400
401
402
403
404
405
406
407
408
409
410
411
412
413
414
415
416
417
418
419
420
421
422
423
424
425
426
427
428
429
430
431
432
433
434
435
436
437
438
439
440
441
442
443
444
445
446
447
448
449
450
451
452
453
454
455
456
457
458
459
460
461
462
463
464
465
466
467
468
469
470
471
472
473
474
475
476
477
478
479
480
481
482
483
484
485
486
487
488
489
490
491
492
493
494
495
496
497
498
499
500
501
502
503
504
505
506
507
508
509
510
511
512
513
514
515
516
517
518
519
520
521
522
523
524
525
526
527
528
529
530
531
532
533
534
535
536
537
538
539
540
541
542
543
544
545
546
547
548
549
550
551
552
553
554
555
556
557
558
559
560
561
562
563
564
565
566
567
568
569
570
571
572
573
574
575
576
577
578
579
580
581
582
583
584
585
586
587
588
589
590
591
592
593
594
595
596
597
598
599
600
601
602
603
604
605
606
607
608
609
610
611
612
613
614
615
616
617
618
619
620
621
622
623
624
625
626
627
628
629
630
631
632
633
634
635
636
637
638
639
640
641
642
643
644
645
646
647
648
649
650
651
652
653
654
655
656
657
658
659
660
661
662
663
664
665
666
667
668
669
670
671
672
673
674
675
676
677
678
679
680
681
682
683
684
685
686
687
688
689
690
691
692
693
694
695
696
697
698
699
700
701
702
703
704
705
706
707
708
709
710
711
712
713
714
715
716
717
718
719
720
721
722
723
724
725
726
727
728
729
730
731
732
733
734
735
736
737
738
739
740
741
742
743
744
745
746
747
748
749
750
751
752
753
754
755
756
757
758
759
760
761
762
763
764
765
766
767
768
769
770
771
772
773
774
775
776
777
778
779
780
781
782
783
784
785
786
787
788
789
790
791
792
793
794
795
796
797
798
799
800
801
802
803
804
805
806
807
808
809
810
811
812
813
814
815
816
817
818
819
820
821
822
823
824
825
826
827
828
829
830
831
832
833
834
835
836
837
838
839
840
841
842
843
844
845
846
847
848
849
850
851
852
853
854
855
856
857
858
859
860
861
862
863
864
865
866
867
868
869
870
871
872
873
874
875
876
877
878
879
880
881
882
883
884
885
886
887
888
889
890
891
892
893
894
895
896
897
898
899
900
901
902
903
904
905
906
907
908
909
910
911
912
913
914
915
916
917
918
919
920
921
922
923
924
925
926
927
928
929
930
931
932
933
934
935
936
937
938
939
940
941
942
943
944
945
946
947
948
949
950
951
952
953
954
955
956
957
958
959
960
961
962
963
964
965
966
967
968
969
970
971
972
973
974
975
976
977
978
979
980
981
982
983
984
985
986
987
988
989
990
991
992
993
994
995
996
997
998
999
1000
1001
1002
1003
1004
1005
1006
1007
1008
1009
1010
1011
1012
1013
1014
1015
1016
1017
1018
1019
1020
1021
1022
1023
1024
1025
1026
1027
1028
1029
1030
1031
1032
1033
1034
1035
1036
1037
1038
1039
1040
1041
1042
1043
1044
1045
1046
1047
1048
1049
1050
1051
1052
1053
1054
1055
1056
1057
1058
1059
1060
1061
1062
1063
1064
1065
1066
1067
1068
1069
1070
1071
1072
1073
1074
1075
1076
1077
1078
1079
1080
1081
1082
1083
1084
1085
1086
1087
1088
1089
1090
1091
1092
1093
1094
1095
1096
1097
1098
1099
1100
1101
1102
1103
1104
1105
1106
1107
1108
1109
1110
1111
1112
1113
1114
1115
1116
1117
1118
1119
1120
1121
1122
1123
1124
1125
1126
1127
1128
1129
1130
1131
1132
1133
1134
1135
1136
1137
1138
1139
1140
1141
1142
1143
1144
1145
1146
1147
1148
1149
1150
1151
1152
1153
1154
1155
1156
1157
1158
1159
1160
1161
1162
1163
1164
1165
1166
1167
1168
1169
1170
1171
1172
1173
1174
1175
1176
1177
1178
1179
1180
1181
1182
1183
1184
1185
1186
1187
1188
1189
1190
1191
1192
1193
1194
1195
1196
1197
1198
1199
1200
1201
1202
1203
1204
1205
1206
1207
1208
1209
1210
1211
1212
1213
1214
1215
1216
1217
1218
1219
1220
1221
1222
1223
1224
1225
1226
1227
1228
1229
1230
1231
1232
1233
1234
1235
1236
1237
1238
1239
1240
1241
1242
1243
1244
1245
1246
1247
1248
1249
1250
1251
1252
1253
1254
1255
1256
1257
1258
1259
1260
1261
1262
1263
1264
1265
1266
1267
1268
1269
1270
1271
1272
1273
1274
1275
1276
1277
1278
1279
1280
1281
1282
1283
1284
1285
1286
1287
1288
1289
1290
1291
1292
1293
1294
1295
1296
1297
1298
1299
1300
1301
1302
1303
1304
1305
1306
1307
1308
1309
1310
1311
1312
1313
1314
1315
1316
1317
1318
1319
1320
1321
1322
1323
1324
1325
1326
1327
1328
1329
1330
1331
1332
1333
1334
1335
1336
1337
1338
1339
1340
1341
1342
1343
1344
1345
1346
1347
1348
1349
1350
1351
1352
1353
1354
1355
1356
1357
1358
1359
1360
1361
1362
1363
1364
1365
1366
1367
1368
1369
1370
1371
1372
1373
1374
1375
1376
1377
1378
1379
1380
1381
1382
1383
1384
1385
1386
1387
1388
1389
1390
1391
1392
1393
1394
1395
1396
1397
1398
1399
1400
1401
1402
1403
1404
1405
1406
1407
1408
1409
1410
1411
1412
1413
1414
1415
1416
1417
1418
1419
1420
1421
1422
1423
1424
1425
1426
1427
1428
1429
1430
1431
1432
1433
1434
1435
1436
1437
1438
1439
1440
1441
1442
1443
1444
1445
1446
1447
1448
1449
1450
1451
1452
1453
1454
1455
1456
1457
1458
1459
1460
1461
1462
1463
1464
1465
1466
1467
1468
1469
1470
1471
1472
1473
1474
1475
1476
1477
1478
1479
1480
1481
1482
1483
1484
1485
1486
1487
1488
1489
1490
1491
1492
1493
1494
1495
1496
1497
1498
1499
1500
1501
1502
1503
1504
1505
1506
1507
1508
1509
1510
1511
1512
1513
1514
1515
1516
1517
1518
1519
1520
1521
1522
1523
1524
1525
1526
1527
1528
1529
1530
1531
1532
1533
1534
1535
1536
1537
1538
1539
1540
1541
1542
1543
1544
1545
1546
1547
1548
1549
1550
1551
1552
1553
1554
1555
1556
1557
1558
1559
1560
1561
1562
1563
1564
1565
1566
1567
1568
1569
1570
1571
1572
1573
1574
1575
1576
1577
1578
1579
1580
1581
1582
1583
1584
1585
1586
1587
1588
1589
1590
1591
1592
1593
1594
1595
1596
1597
1598
1599
1600
1601
1602
1603
1604
1605
1606
1607
1608
1609
1610
1611
1612
1613
1614
1615
1616
1617
1618
1619
1620
1621
1622
1623
1624
1625
1626
1627
1628
1629
1630
1631
1632
1633
1634
1635
1636
1637
1638
1639
1640
1641
1642
1643
1644
1645
1646
1647
1648
1649
1650
1651
1652
1653
1654
1655
1656
1657
1658
1659
1660
1661
1662
1663
1664
1665
1666
1667
1668
1669
1670
1671
1672
1673
1674
1675
1676
1677
1678
1679
1680
1681
1682
1683
1684
1685
1686
1687
1688
1689
1690
1691
1692
1693
1694
1695
1696
1697
1698
1699
1700
1701
1702
1703
1704
1705
1706
1707
1708
1709
1710
1711
1712
1713
1714
1715
1716
1717
1718
1719
1720
1721
1722
1723
1724
1725
1726
1727
1728
1729
1730
1731
1732
1733
1734
1735
1736
1737
1738
1739
1740
1741
1742
1743
1744
1745
1746
1747
1748
1749
1750
1751
1752
1753
1754
1755
1756
1757
1758
1759
1760
1761
1762
1763
1764
1765
1766
1767
1768
1769
1770
1771
1772
1773
1774
1775
1776
1777
1778
1779
1780
1781
1782
1783
1784
1785
1786
1787
1788
1789
1790
1791
1792
1793
1794
1795
1796
1797
1798
1799
1800
1801
1802
1803
1804
1805
1806
1807
1808
1809
1810
1811
1812
1813
1814
1815
1816
1817
1818
1819
1820
1821
1822
1823
1824
1825
1826
1827
1828
1829
1830
1831
1832
1833
1834
1835
1836
1837
1838
1839
1840
1841
1842
1843
1844
1845
1846
1847
1848
1849
1850
1851
1852
1853
1854
1855
1856
1857
1858
1859
1860
1861
1862
1863
1864
1865
1866
1867
1868
1869
1870
1871
1872
1873
1874
1875
1876
1877
1878
1879
1880
1881
1882
1883
1884
1885
1886
1887
1888
1889
1890
1891
1892
1893
1894
1895
1896
1897
1898
1899
1900
1901
1902
1903
1904
1905
1906
1907
1908
1909
1910
1911
1912
1913
1914
1915
1916
1917
1918
1919
1920
1921
1922
1923
1924
1925
1926
1927
1928
1929
1930
1931
1932
1933
1934
1935
1936
1937
1938
1939
1940
1941
1942
1943
1944
1945
1946
1947
1948
1949
1950
1951
1952
1953
1954
1955
1956
1957
1958
1959
1960
1961
1962
1963
1964
1965
1966
1967
1968
1969
1970
1971
1972
1973
1974
1975
1976
1977
1978
1979
1980
1981
1982
1983
1984
1985
1986
1987
1988
1989
1990
1991
1992
1993
1994
1995
1996
1997
1998
1999
2000
2001
2002
2003
2004
2005
2006
2007
2008
2009
2010
2011
2012
2013
2014
2015
2016
2017
2018
2019
2020
2021
2022
2023
2024
2025
2026
2027
2028
2029
2030
2031
2032
2033
2034
2035
2036
2037
2038
2039
2040
2041
2042
2043
2044
2045
2046
2047
2048
2049
2050
2051
2052
2053
2054
2055
2056
2057
2058
2059
2060
2061
2062
2063
2064
2065
2066
2067
2068
2069
2070
2071
2072
2073
2074
2075
2076
2077
2078
2079
2080
2081
2082
2083
2084
2085
2086
2087
2088
2089
2090
2091
2092
2093
2094
2095
2096
2097
2098
2099
2100
2101
2102
2103
2104
2105
2106
2107
2108
2109
2110
2111
2112
2113
2114
2115
2116
2117
2118
2119
2120
2121
2122
2123
2124
2125
2126
2127
2128
2129
2130
2131
2132
2133
2134
2135
2136
2137
2138
2139
2140
2141
2142
2143
2144
2145
2146
2147
2148
2149
2150
2151
2152
2153
2154
2155
2156
2157
2158
2159
2160
2161
2162
2163
2164
2165
2166
2167
2168
2169
2170
2171
2172
2173
2174
2175
2176
2177
2178
2179
2180
2181
2182
2183
2184
2185
2186
2187
2188
2189
2190
2191
2192
2193
2194
2195
2196
2197
2198
2

sulfites, bisulfites, metabisulfite, or other inorganic salts and acids containing sulfur.

11. Skin warming agents: Examples include vanillyl
5 butylamid, capsaicin and mixtures thereof.

10 The secondary component enhances the dermatological benefits achieved by the PPAR Stabilizer. The compositions of the present invention may include at least two secondary components, with each secondary component being selected from a different group.

15 The compositions of the present invention can include other cosmetic and pharmaceutical actives and excipients. Such suitable cosmetic and pharmaceutical agents include, but are not limited to, one or more of erythromycins, tetracyclines, salicylic acids, antifungals, vitamins, anti-inflammatory agents, antimicrobials, analgesics, nitric oxide synthase inhibitors, insect repellents, self-tanning agents, surfactants, 20 moisturizers, stabilizers, preservatives, antiseptics, chelating agents, thickeners, emulsifiers, lubricants, humectants, chelating agents, skin penetration enhancers, skin cooling agents, emollients, fragrances and colorants.

Examples of suitable thickening agents include xanthan gum, hydroxypropyl cellulose, hydroxyethyl cellulose, carbomer, gum acacia, Seppigel 305 (available from Seppic Co., France), and magnesium aluminum silicate.

5

The topical compositions of the present invention can include, and their utility can be enhanced by, one or more of humectants, such as ureas, pyrrolidone carboxylic acids, amino acids, sodium hyaluronates, certain polyols and other compounds with hygroscopic properties.

10
15
20
25
30
35
40
45
50
55
60
65
70
75
80
85
90
95
100
105
110
115
120
125
130
135
140
145
150
155
160
165
170
175
180
185
190
195
200
205
210
215
220
225
230
235
240
245
250
255
260
265
270
275
280
285
290
295
300
305
310
315
320
325
330
335
340
345
350
355
360
365
370
375
380
385
390
395
400
405
410
415
420
425
430
435
440
445
450
455
460
465
470
475
480
485
490
495
500
505
510
515
520
525
530
535
540
545
550
555
560
565
570
575
580
585
590
595
600
605
610
615
620
625
630
635
640
645
650
655
660
665
670
675
680
685
690
695
700
705
710
715
720
725
730
735
740
745
750
755
760
765
770
775
780
785
790
795
800
805
810
815
820
825
830
835
840
845
850
855
860
865
870
875
880
885
890
895
900
905
910
915
920
925
930
935
940
945
950
955
960
965
970
975
980
985
990
995

The general activity and mildness to skin of the present topical compositions can also be enhanced by neutralization to pH about 3.5 to about 7.0, most preferably from pH about 3.7 to about 5.6. This neutralization is preferably accomplished with one or more of ammonium hydroxide, potassium hydroxide, sodium hydroxide, arginine or other amino acids, and/or triethanolamine.

20

The topical compositions of the present invention can be further formulated according to procedures known in the art to provide cosmetic compositions such as emulsions, gels, creams, lotions, ointments, pastes, sticks, cakes, pencils, essences and serums, as well as other topical cosmetic vehicles. It is also

contemplated that topical compositions of the present invention can be incorporated into delivery systems such as liposomes and topical patches, tapes, and sprays.

5 PPAR STABILIZERS

The topical compositions of the present invention are useful to improve the aesthetic appearance of skin, particularly teen skin, by any one of the following methods:

1. Reducing oil production by sebaceous glands;
- 10 2. Reducing lipid synthesis in subcutaneous adipose tissue;
3. Reducing triglyceride synthesis in subcutaneous adipose tissue;
- 15 4. Preventing and/or improving skin conditions associated with nonselective or partially selective PPAR stimulators/upregulators;
5. Preventing, ameliorating or treating acne;
6. Preventing, ameliorating or treating oily skin;
7. Preventing, ameliorating or treating oily hair;
- 20 8. Preventing, ameliorating or treating oily scalp;
9. Preventing, ameliorating or treating cellulite; and
10. Preventing, ameliorating or treating blemishes;
11. Preventing, ameliorating or treating breakouts; and
12. Improving skin texture.

The foregoing methods are achieved by topically applying an effective amount of a PPAR Stabilizer in a topical composition, to affected areas. Preferably the PPAR Stabilizer is perilla oil and, more preferably, the perilla oil is derived from the perilla seed, i.e. perilla seed oil,.

As discussed above, the discovery that perilla oil is useful as a PPAR stabilizer is an unexpected discovery in light of the prior art. It is very surprising that perilla oil as a source of linolenic acid and linoleic acid (known non-selective PPAR agonists) can prevent upregulation of PPAR, thereby providing a positive effect on acne and cellulite.

When the PPAR Stabilizer is perilla oil, the PPAR Stabilizer may be directly applied to the affected area. It is preferred that the PPAR Stabilizer is incorporated into a topical composition in an amount from about 0.01 wt% to about 10 wt%. More preferably, the PPAR Stabilizer is incorporated into the topical composition in an amount from about 1 wt% to about 8 wt%. It is most preferred that the PPAR Stabilizer is incorporated into the topical composition in an amount from about 3 wt% to about 6 wt%.

As can be understood by those in the art, the number of applications per day may vary upon the concentration of PPAR Stabilizer in the topical composition, as well as the nature of the vehicle of the topical composition, such as a gel versus a topically applied patch. When the topical composition has from about 0.01 wt% to about 10 wt% perilla oil in a cream vehicle, it is believed that such a composition should, preferably, be applied one to three times a day for acne conditions and one to two times a day for cellulite conditions. When such a topical composition is used to improve the overall aesthetic appearance of skin, it is preferred that the topical composition is applied one to two times a day.

When the condition to be treated is cellulite located on the thigh, the topical composition should be applied directly on the area. When the condition to be treated is oily scalp, the topical composition may be in the form of a shampoo or conditioner. When the condition is oily hair, the topical composition may additionally be in the form of a styling gel, hair spray or leave-in conditioner.

When the condition to be treated is acne, the composition may include: perilla oil having alpha-linolenic acid, eicosapentaenoic acid, and a suitable vehicle. However, it is preferred that the weight ratio of eicosapentaenoic acid to alpha-linolenic acid is outside the range of 1:0.1 to 20. Fish oil is a known and suitable source of eicosapentaenoic acid. When fish oil is the source of eicosapentaenoic acid, it is preferred that the fish oil includes less than 5 wt% or greater than 40 wt% eicosapentaenoic acid and the perilla oil includes less than 30 wt% or greater than 70 wt% of alpha-linolenic acid. Also, it is preferred that the volume of fish oil in the composition is either less than one-tenth the volume of perilla oil in the composition or greater than ten times the volume of perilla oil in the composition.

The following examples are illustrative of the present invention and are not intended to limit the invention.

EXAMPLE 1

Human skin cells were used to determine the effect upon PPAR upregulation by known PPAR agonists and the compound of the present invention as measured by relative PPRE ("Peroxisome Proliferator Response Element") activity. Preconfluent keratinocytes were transiently transfected with a

PPRE-luciferase reporter construct together with a beta-galactosidase. Four similar groups of cells were treated the following day for 24 hours. The first group contained a vehicle having 0.05% dimethyl sulfoxide (DMSO). The second group was treated with G3, a PPAR alpha agonist. The third group was treated with A4, perilla seed oil diluted 1:100 with DMSO. The fourth group was treated with G3 and A4.

As the results illustrated in Figure 1 show, the addition of a PPAR agonist (G3) nearly doubled the PPRE activity as compared to the vehicle. The addition of perilla seed oil (A4) completely prevented the upregulation of PPAR in the presence of G3.

EXAMPLE 2

As in Example 1, confluent keratinocytes were transfected with PPRE-luciferase and beta-galactosidase. Six similar groups of cells were treated the following day for 24 hours. The first group contained a vehicle having 0.05% DMSO. The second group was treated with A5, perilla seed oil diluted 1:100 with DMSO. The third group was treated with farnesol, a PPAR activator. The fourth group was treated with farnesol and A5. The fifth group was treated with an analog of clofibrate, a known PPAR alpha agonist. The sixth group was treated with the clofibrate analog and A5. As the results illustrated in Figure

2 show, the addition of A5 to cells treated with the PPAR agonists significantly prevents PPAR upregulation. In fact, even in the presence of such agonists, A5 maintains PPRE activity in the range exhibited by the vehicle alone.

5

Various modifications and alterations to the present invention may be appreciated based on a review of this application. These changes and additions are intended to be within the scope and the spirit of the present invention as defined by the following claims.

10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60
61
62
63
64
65
66
67
68
69
70
71
72
73
74
75
76
77
78
79
80
81
82
83
84
85
86
87
88
89
90
91
92
93
94
95
96
97
98
99
100

CLAIMS

What is claimed is:

1. A method of treating or ameliorating an affected area
5 of the skin or hair comprising topically applying to the
affected area a PPAR stabilizer in an amount effective to
improve the aesthetic appearance of the affected area.

2. The method of claim 1, wherein the PPAR stabilizer is
10 perilla oil.

3. The method of claim 2, wherein the perilla oil is
perilla seed oil.

4. The method of claim 1, wherein the affected area of
15 the skin or hair is in a non-disease state and exhibits
characteristics associated with a condition selected from the
group consisting of: one or more blemishes, skin breakouts,
cellulite, oily skin, oily hair, oily scalp, and any combination
20 thereof.

5. The method of claim 4, wherein the condition is
cellulite.

6. The method of claim 4, wherein the condition is oily skin.

7. The method of claim 4, wherein the condition is oily hair or oily scalp.

8. The method of claim 4, wherein the condition is one or more blemishes.

9. The method of claim 4, wherein the condition is skin break out.

10. The method of claim 4, wherein the topical composition comprises from about 0.01 wt% to about 10 wt% of the PPAR stabilizer.

11. The method of claim 10, wherein the topical composition comprises from about 1 wt% to about 8 wt% of the PPAR stabilizer.

12. The method of claim 4 wherein the PPAR stabilizer is perilla oil.

13. The method of claim 5, wherein the PPAR stabilizer is perilla oil.

14. A method of treating skin affected by acne comprising:
5 preparing a topical composition including: perilla oil
having alpha-linolenic acid, and a suitable vehicle, and
wherein the composition is applied in the absence of from
0.1 to 20 times of an amount of alpha-linolenic acid, based upon
the weight of the eicosapentaenoic acid in the composition.

15. The method of claim 14, wherein the eicosapentaenoic
acid is provided by fish oil having less than 5% or greater than
40% eicosapentaenoic acid, and the perilla oil comprises less
than 30% or greater than 70% of alpha-linolenic acid.

16. The method of claim 14, wherein the topical composition
further comprises a secondary component selected from the group
consisting of:

- an estrogen synthetase stimulating compound;
- 20 a 5 alpha-reductase activity inhibiting compound;
- an exfoliation-promoting compound;
- an ultraviolet (UV) light protecting/sunscreen agent;
- a retinoid;
- a rexinoid;

a barrier function enhancing agent;
a collagen enhancing agent;
an elastase inhibitor;
a skin lightening agent;
5 an antioxidant;
a skin warming agent; and
any mixtures thereof.

17. The method of claim 14, wherein the topical
10 composition further comprises a secondary component selected
from the group consisting of:

an exfoliation-promoting compound;
an ultraviolet (UV) light protecting/sunscreen agent;
a retinoid;
15 a rexinoid;
a collagen enhancing agent;
an elastase inhibitor; and
any mixtures thereof.

20 18. A method of preventing, ameliorating or treating a
condition selected from the group consisting of blemishes,
breakout, cellulite, oily skin, oily hair, oily scalp, and a
combination thereof, comprising topically applying perilla oil
to an area of skin or hair affected by the condition in an

amount effective to improve the aesthetic appearance of the condition.

19. The method of claim 18, wherein the condition is
5 cellulite, and the perilla oil is applied to the affected area of skin.

20. A method of treating a skin or hair condition
resulting from or accompanied by an upregulation of PPAR
10 receptors comprising:

topically applying perilla oil to the condition,

wherein the condition is selected from the group consisting
of cellulite, oily skin, oily hair, oily scalp, and a
combination thereof.

ABSTRACT OF THE DISCLOSURE

5 skin, oily hair, oily scalp, or any combination thereof, that comprises topically applying an effective amount of perilla oil to the affected area of the skin or hair. The topical application of perilla oil inhibits PPAR upregulation in skin cells, particularly PPARalpha upregulation.

10

[illegible]

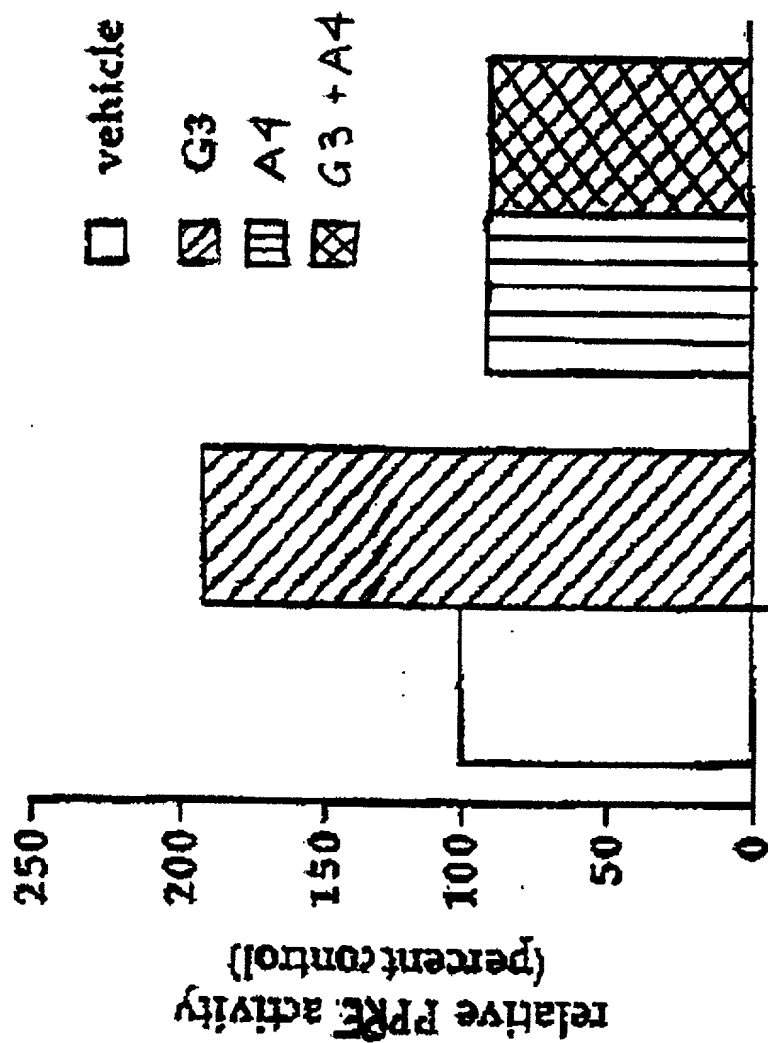


FIGURE 1

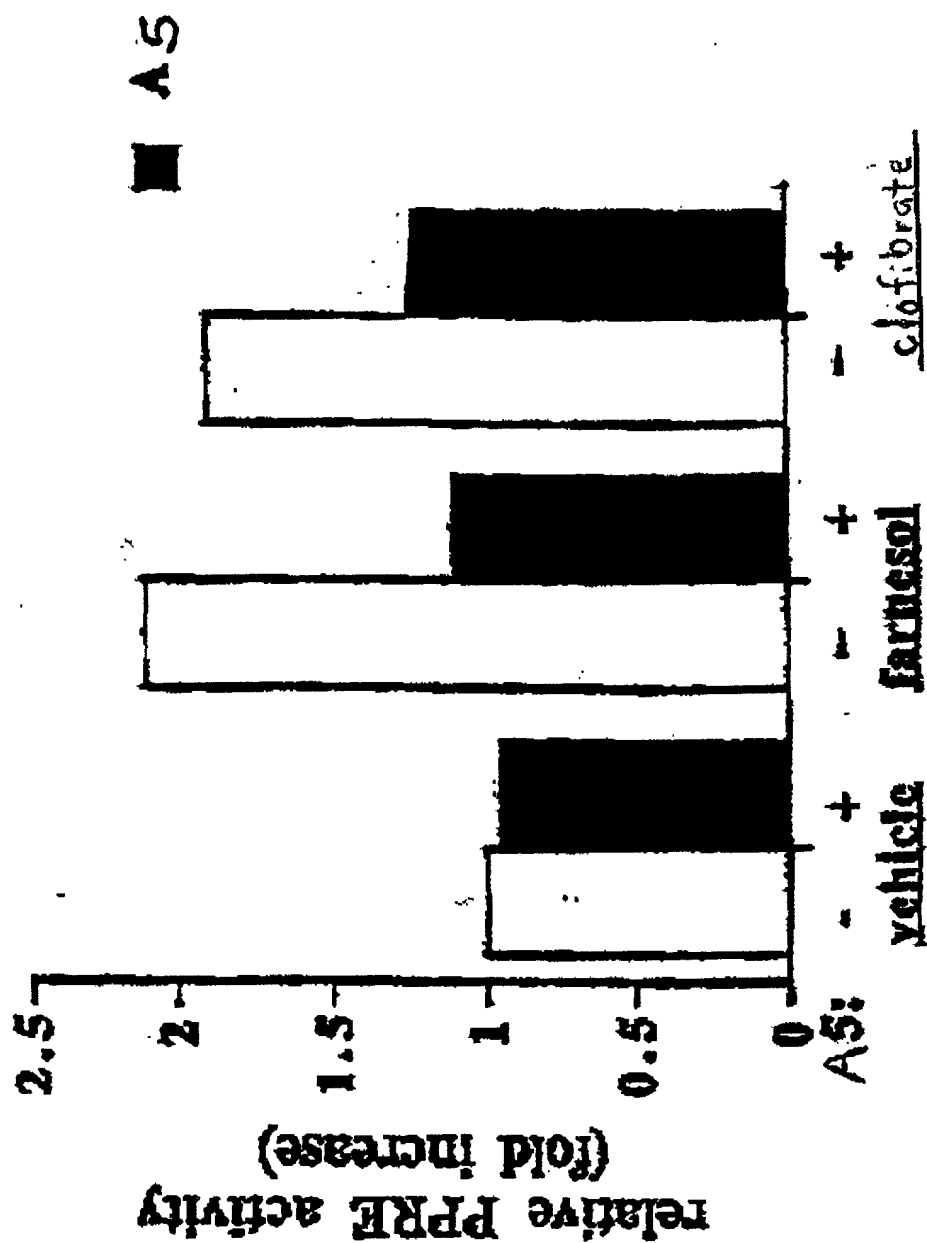


FIGURE 2

DECLARATION AND POWER OF ATTORNEY FOR PATENT APPLICATIONDocket No. 680.0035USU

As a below named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated below next to my name.

I believe I am the original, first and sole inventor of the subject matter that is claimed and for which a patent is sought on the invention entitled.

METHOD OF TREATING SKIN CONDITIONS

the specification of which

(check one) XX is attached hereto. was filed on as Application Serial No and was amended on (if applicable).

I hereby state that I have reviewed and understand the contents of the above-identified specification, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose to the U.S. Patent and Trademark Office all information known to me to be material to the examination of this application as defined in Title 37, Code of Federal Regulations, §1.56.

I hereby claim foreign priority benefits under Title 35, United States Code, §119 of any foreign application(s) for patent or inventor's certificate(s) listed below and have also identified below any foreign application(s) for patent or inventor's certificate(s) having a filing date before that of the application on which priority is claimed:

Prior Foreign Application(s)**Priority Claimed**

<u> </u> (Number)	<u> </u> (Country)	<u> </u> (Day/Mon/Year Filed)	<u> </u> Yes <u> </u> No
<u> </u> (Number)	<u> </u> (Country)	<u> </u> (Day/Mon/Year Filed)	<u> </u> Yes <u> </u> No
<u> </u> (Number)	<u> </u> (Country)	<u> </u> (Day/Mon/Year Filed)	<u> </u> Yes <u> </u> No

I hereby claim the benefit under Title 35, United States Code, §120 of any United States application(s) listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States application in the manner provided by the first paragraph of Title 35, United States Code, §112, I acknowledge the duty to disclose material information as defined in Title 37, Code of Federal Regulations, §1.56(a) which occurred between the filing date of the prior application and the national or PCT international filing date of this application:

(Application Serial No.) (Filing Date) Status
(patent, pend., abandon.)

(Application Serial No.) (Filing Date) Status
(patent, pend., abandon.)

(Application Serial No.) (Filing Date) Status
(patent, pend., abandon.)

POWER OF ATTORNEY: As a named inventor, I hereby appoint the following attorney(s) and/or agent(s) to prosecute this application and transact all business in the Patent and Trademark Office connected therewith.

NAMES	REGISTRATION NUMBERS
Charles N.J. Ruggiero	28,468
Paul D. Greeley	31,019
Harry F. Smith	32,493

SEND CORRESPONDENCE TO:	DIRECT TELEPHONE CALLS TO:
Charles N.J. Ruggiero, Esq. Ohlandt, Greeley, Ruggiero & Perle One Landmark Square, 9 th Floor Stamford, Connecticut 06901	Charles N.J. Ruggiero, Esq. (203) 327-4500 (203) 327-6401

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

FULL NAME OF INVENTOR	LAST NAME MENON	FIRST NAME GOPINATHAN	MIDDLE NAME K.
RESIDENCE & CITIZENSHIP	CITY WAYNE	STATE OR COUNTRY NEW JERSEY	CITIZENSHIP INDIA
POST OFFICE ADDRESS	P.O. ADDRESS 9 MILLER ROAD	CITY & STATE WAYNE, NEW JERSEY	ZIP CODE 07470

Inventor's signature


Gopinathan K. Menon

Date MARCH 7th, 2000